



## C. T. guided fine needle aspiration cytology of localised lung lesions : cytological versus radiological correlation

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### ABSTRACT

**Background and Objectives:** Lung tumors accounts for various benign and malignant conditions. Lung cancer is the most frequent and one of the most deadly cancer types with more than 1.6 million deaths annually worldwide. The present study was undertaken to know the cytomorphological spectrum of localised lung lesions and its correlation with radiological findings.

**Materials and Methods:** The present study was conducted in the Department of Pathology, Tuberculosis and Chest Diseases & Radiodiagnosis at S.N. Medical College, Agra on 66 patients over an 36 months period. Computed tomography (CT) guided fine needle aspiration cytology (FNAC) was carried out, and aspirates were drawn, examined, and compared with their radiological diagnoses.

**Results:** A total of 66 cases presented as localised lung masses out of which 64 cases (96.9%) were consistent with malignancy, and 2 cases (3.1%) benign on clinical and radiological evaluation. On cytological evaluation of 66 cases, 62 cases (93.8%) were considered malignant, 2 (3.1%) of them benign and 2 cases (3.1%) were inadequate for diagnosis. The diagnostic adequacy in current series is 97.0%. Complications were infrequent and included pneumothorax in 4 (6.1%) cases. By cytology, the most common malignant lesion was adenocarcinoma (42.2%) followed by squamous cell carcinoma (31.2%), adenosquamous carcinoma (6.2%), and lymphoid neoplasm (4.7%). Radiological findings were consistent with cytomorphological findings in all cases.

**Conclusion:** Present study thus concludes that CT guided FNA of thoracic lesions is a simple, safe, economically prudent technique associated with low morbidity and leading to quick and early diagnosis. Conclusive diagnosis on FNAC obviates the need for open biopsies.

**KEYWORDS :** Lung carcinoma, Primary Neoplasm, Metastatic deposit, Percutaneous CT guided FNAC, Pulmonary Nodule

### Introduction

Lung lesions include a large variety of benign and malignant conditions. Lung carcinoma is the most common carcinoma in the world today, comprising 12.6% of all the cancers and 17.8% of all the cancer deaths.<sup>[1]</sup> Benign lesions include inflammatory conditions comprising of acute Inflammatory conditions, granulomatous inflammation, specific infections ( Aspergillus, Phycomycetes, Fusarium, Candida ), reparative and reactive changes, pneumoconiosis, pulmonary infarct, congenital bronchogenic cyst, nodular amyloidosis and wegenger's granulomatosis. Neoplastic lesions includes primary and secondary neoplasms. Primary neoplasm includes squamous cell carcinoma, adenocarcinoma, lepidic adenocarcinoma, small cell carcinoma, large cell carcinoma, carcinoid tumour, sarcomatoid carcinoma and adenosquamous carcinoma. Other rare primary tumors includes pulmonary blastoma and pulmonary carcinosarcoma.

Lung is a well-known common site for metastatic tumors.<sup>[2,3]</sup> Although clinical data, location, and radiological findings can narrow down the diagnostic possibilities, cytological diagnosis is warranted before initiating the specific treatment for malignant diseases.<sup>[4]</sup> Percutaneous CT-guided fine needle aspiration cytology (FNAC) is considered to be the first choice for the initial investigation and diagnosis of superficial and deep lesions, especially in lesions which are in pulmonary apex, upper lobe, medial lobe and periphery, particularly small lesions (one centimeter or so in diameter).<sup>[5]</sup> With the additional information provided by CT and with established fine needle techniques, biopsy can be performed for previously non-visualized or less accessible lesions in lung, pleura, and mediastinum.<sup>[6]</sup>

In an attempt to determine the nature of pulmonary nodule (benign versus malignant), clinical data alone do not allow a definite diagnosis. Therefore radiological evaluation with C.T. plays an important role in understanding the characteristic of the lesion such as size, location, contour, edge and density (including presence and absence of calcification or fat). Unfortunately none of these features alone help in establishing benignity or malignancy and significant overlap exists among various lesions and in these cases role of cytology is a boon.<sup>[5]</sup>

Localised lung lesions may be benign also and it is a common radiologic abnormality often detected incidentally.<sup>[7]</sup> However, a solitary nodule may also potentially represent an early stage of lung cancer or a metastasis. Diagnostic procedures such as CT guided fine needle aspiration biopsy can exclude malignancy in a majority of cases and may eliminate the need for more invasive surgical procedure.

In a developing country like India and especially in our north eastern region, the poor resources of health care facilities limit us to rely on cytomorphological features and even patients are reluctant for further advanced invasive procedures. Most of the patients presenting in advanced stages of disease and in such cases diagnostic thoracotomy is not advisable and diagnosis is usually established based on small biopsy and cytology specimens. Recently, the 2015 world health organization (WHO) classification of lung tumors is the first WHO classification to provide standardized criteria and terminology for lung cancer diagnosis in small biopsies and cytology.<sup>[8]</sup>

The purpose of this study is to evaluate the utility and complications

of CT guided aspiration cytology in localised lung lesions and to know the pathological spectrum of localised lung lesions along with the correlation of CT findings with cytomorphological reports.

**Aims & objectives**

1. To study the cytological characteristics of various localised lung lesions subjected to FNAC and its correlation with C.T. findings.
2. To study the adequacy of aspirates obtained from localised lung lesions by fine needle aspiration under C.T. guidance.
3. To study the complications consequent upon the procedure.
4. To study the various problems encountered in cytodagnosis of these aspirates.

**Material and Methods**

The present study was conducted in Department of Pathology, Tuberculosis and Chest Diseases & Radiodiagnosis at S.N. Medical College, Agra. Fine needle aspiration smears from the cases of localised lung lesions aspirated under computed tomography guidance were received in the cytology section of department of pathology for cytological evaluation.

The criterion for selection of patients was as follows:-

- (1) Patients with localised lung lesions on chest x-ray and CT were included in the study.
- (2) Patients were co-operative and were able to hold breath for a short while.
- (3) Patient had no bleeding tendency or coagulopathy.

Plain and contrast CT of chest was done as an out patient procedure after explaining the risks and benefits and obtaining informed consent.

First, an axial scan of area of interest only, was done to locate the lesion. The best approach (supine or prone) was judged and the skin puncture site was marked with a radio-opaque dye marker. After cleaning and draping, local anaesthetic (2% xylocaine) was infiltrated at the site of puncture. A 22 – 23 gauge spinal needle was then inserted during suspended respiration, directing the tip of the needle towards the lesion, when the tip of the needle was located in the outer edge of the lesion, a repeat slice of the area of interest was taken to check the exact position of its tip.

The stylet was then withdrawn 2 – 3 cm and the needle was then advanced into the mass with a rotating motion during suspended respiration, so that the tip lied within the target lesions at all times. 20 ml syringe was attached to the needle's hub and the plunger was pulled back, and during the continued hard suction, the needle was jiggled to free material from the lesion into the needle's lumen.

The aspirated material was expelled into the clean glass slides and smears were prepared. Air dried smears were fixed in methanol for 20 – 30 minutes and then stained with May – Grunwald Giemsa stain. After drying the smears were mounted with DPX and then scrutinized under the microscope.

A repeat slice in the area of interest was taken to rule out pneumothorax or bleeding in the needle tract.

The cytological diagnoses were rendered. The radiological opinion of each individual lesion was also recorded. Both cytological and radiological opinions were tabulated and compared statistically.

**Results**

A total of 66 fine needle aspiration smears from the cases of localised lung lesions aspirated under computed tomography guidance were received in the cytology section of department of pathology for cytological evaluation.

**Sex groups**

A total of 66 aspirates were performed, out of which 55 (83.3%) were males and 11 (16.7%) were females.

**Age groups**

Of the total 66 cases, the age of the patients in the present study varied from 25 years to 85 years. 9 Groups were made from 0 – 10 years to 81 – 90 years.

**Table I: DISTRIBUTION OF CASES ACCORDING TO AGE AND CYTOLOGICAL DIAGNOSIS IN VARIOUS GROUPS**

S. No.	Age Groups	No. of Cases	Various Lesions – Diagnosed	%
1.	0 – 10	00	-	0.0
2.	11 – 20	00	-	0.0
3.	21 – 30	02	Adenocarcinoma	3.0
4.	31 – 40	01	NH – SRCN*	1.5
5.	41 – 50	10	Resolving phase of pneumonia, Adenocarcinoma, SCC**, Sq CC, Mets-adenocarcinoma, LCC***	15.2
6.	51 – 60	25	Adenocarcinoma, NHL, Sq.CC, ASqC, GCC***, LCC***, inadequate	37.9
7.	61 – 70	15	Sq.CC, Adenocarcinoma, ASqC, Granulomatous inflammation	22.7
8.	71 – 80	10	Sq.CC, Adenocarcinoma, Adenocarcinoma with lepidic pattern, ASqC, Malignant Mesothelioma	15.2
9.	81 – 90	03	Adenocarcinoma, inadequate, SqCC	4.5
	TOTAL	66		100.0

\* SCC: Small Cell Carcinoma, \*\*\* LCC: Large Cell Carcinoma, \* NH – SRCN: Non-hematolymphoid small round cell neoplasm, \*\*\*GCC:Giant Cell Carcinoma

Of these 64 cases, 2 cases (3.1%) were benign with the diagnoses of resolving phase of pneumonia and granulomatous inflammation. The maximum number of 25 cases (37.9%) lay in the age group of 51 – 60 years, followed by 15 cases (22.7%) in the age group 61 – 70 years and 10 cases (15.2%) in the age group of 41 – 50 years and 71 – 80 years.

**Adequacy**

The aspirates were considered adequate if the cellular elements were sufficient for rendering the diagnosis. The aspirates were considered inadequate (a total of 2 of 66 cases i.e. 3.0%) when they comprised only blood with few nonspecific cellular elements or a variety of normal cell types or few atypical cells, but not suggestive of any specific diagnosis. The smears of 64 cases (97.0%) were adequate and specific non neoplastic and neoplastic diagnoses were rendered.

**Cytological diagnosis**

The breakup of 64 cases which were adequate for cytological diagnosis on fine needle aspiration was:-

1. Non neoplastic cases – 02 (3.1%)
2. Neoplastic (all malignant) cases – 62 (96.9%)

**Table II: DISTRIBUTION ACCORDING TO CYTOLOGICAL DIAGNOSIS**

S.	Cytological Diagnosis	No. of Cases	%
1.	Non Neoplastic (Resolving phase of pneumonia, Granulomatous inflammation)	2	3.1
2.	Neoplastic		
	a. Benign	0	0.0
	b. Malignant		
	i. Squamous cell carcinoma	20	31.2
	ii. Small cell carcinoma	1	1.6
	iii. Adenocarcinoma	26	40.6
	• Conventional	1	1.6
	• Adenocarcinoma with lepidic pattern		
	iv. Large cell carcinoma	2	3.1
	v. Adenosquamous carcinoma	4	6.2
	vi. Giant cell carcinoma	1	1.6
	vii. Lymphoid Neoplasm	3	4.7
	viii. Malignant mesothelioma	1	1.6

	ix.	Non - Hematolymphoid small round cell neoplasm (possibly Askin tumour)	1	1.6
	x.	Metastatic Adenocarcinoma	2	3.1
		TOTAL	64	100.0

- Squamous cell carcinoma - Ragged cluster margin, anisochromasia, hyperchromatic nucleus, evidence of keratinization, necrotic background.(Fig. 1a &1b and Fig. 2a &2b)
- Adenocarcinoma – Cell aggregates( sheets, rosettes and acinar groupings), rounded nuclei, prominent nucleoli, clean or mucinous background.(Fig. 3a & 3b and fig. 5a & 5b)
- Adenocarcinoma with lepidic pattern – Flat sheets, papillae, cell balls, acini, intra-nuclear inclusions and grooving.
- Small cell carcinoma – Artificially crushed cells and nuclei, fragile small round cells with extremely scant cytoplasm, stippled chromatin, nuclear moulding.(Fig. 4a &4b)
- Giant cell carcinoma – Numerous multinucleated loosely cohesive neoplastic giant cells, neutrophil emperipolesis and granular necrotic inflammatory background.
- Large cell carcinoma – Loose cohesion as well as dispersal, large pleomorphic malignant cells, scattered multinucleate tumour giant cells with inflammatory background.
- Adenosquamous Carcinoma – Features of dual differentiation (glandular as well as squamous).
- Metastatic renal cell carcinoma – Aggregates of cells with abundant granular or clear cytoplasm, rounded nuclei and macronucleoli.

Comparison of malignant lesions reported in Cytologic literature vs current study:-

**Table III : COMPARISON OF MALIGNANT LESIONS**

S. No.	Malignant lesions	Literature (%)	Present study (%)
1.	Squamous cell carcinoma	12.5 - 58.3	31.2
2.	Small cell carcinoma	1.5 - 34.1	1.6
3.	Adenocarcinoma(Bronchogenic)	14.6 - 54.2	40.6
4.	Adenocarcinoma with lepidic pattern	1.0 - 5.0	1.6
5.	Large cell carcinoma	1.1 - 7.3	3.1
6.	Adenosquamous carcinoma	0.4 - 0.7	6.2
7.	Giant cell carcinoma	0.0 - 0.0	1.6
8.	Lymphoid neoplasm	0.7 - 6.1	4.7
9.	Malignant mesothelioma	0.0 - 3.8	1.6
10.	Non-hematolymphoid small round cell neoplasm	0.0 - 0.0	1.6
11.	Metastatic adenocarcinoma	1.1 - 29.1	3.1

**RADIOLOGICAL AND CYTOLOGICAL CORRELATION**

In our present study, 66 cases having localised lung lesions (as seen by computed tomography) were aspirated under CT guidance. The size of the lesions varied from 2.6 x 2.3 cm to 10.7 x 10.3 cm (mean 7.1 x 5.3 cm).

The radiological impression in most of the masses was of an irregular outlined, heterogeneously enhancing iso to hypodense mass(FIG.40); some of them showing extension into the adjacent structures. Frequent association of mediastinal lymphadenopathy was noted. At times, mass affect or infiltration of bronchial tree and major vessels were observed. There was evidence of lymphangitic spread as suggested by nodular and septal thickening in sub pleural or subfissural and peribronchovascular location.

6 cases (9.1%) presented with nodular thickening of pleura or pleural effusion along with a mass. All these lesions were considered to be malignant lesions radiologically and FNAC was recommended for further confirmation.

Of all the 66 cases, 2 cases (3.0%) were known cases of carcinoma and were on chemotherapy / radiotherapy. One was a known case of squamous cell carcinoma and the other was a known case of

adenocarcinoma.

4 cases (6.1%) presented with metastatic lesions in liver.

6 cases (9.1%) presented with infiltrative findings (e.g. rib destruction), pleural effusion and symptoms of nerve and vessel involvement.

**TableIII: CORRELATION OF RADIOLOGICAL WITH CYTOLOGICALDIAGNOSIS**

S. No.	Cytological Diagnosis	Radiological Diagnosis	No. of Cases	%
1.	Non Neoplastic (resolving phase of pneumonia, granulomatous inflammation)	Localised lung masses ?? Malignancy ?? Consolidation	2	3.0
2.	Neoplastic • Benign neoplasm • Malignant neoplasm • Adequate with specific diagnosis • Adequate but no diagnosis conferred	Neoplastic ? Malignant	0 62 0	0.0 94.0 0.0
3.	Inadequate	?? Neoplastic	2	3.0
	Total		66	100.0

**DISCUSSION**

A total of 66 cases presented as localised lung masses out of which 64 were consistent with malignancy, and 2 cases benign on clinical and radiological evaluation. On cytological evaluation of 66 cases, only 62 cases were considered malignant, 2 of them benign and 2 cases were inadequate for diagnosis.

The adequacy rate in the present series is 97%, the values were very near the values of Madan M. et al (95.0%),<sup>[9]</sup> Sarker R. N. et al (95.0%)<sup>[10]</sup> and Rangaswamy M. et al (96.3%).<sup>[11]</sup> Other workers have reported diagnostic yield ranging from 44% to 96.3% when fine needle aspiration cytology was combined with imaging modalities i.e. computed tomography.

In the current study lesions were divided into non-malignant which accounted for 2 of 64 cases (3.1%) and malignant lesions, which accounted for 62 of 64 cases (96.9%). The distribution of benign and malignant lesions in the literature varied from, 7.8% - 37.8% for benign and 62.2% - 96.3% for malignant cases. Our findings were very near to the study of Shaheen M.Z. et al (2006)<sup>[12]</sup> and Yilmaz A. et al (2002).<sup>[13]</sup> In the present study, there was a disproportionately high figure for malignant cases as compared to other series; maximum of the latter were from outside India. This could be attributable to the fact that our's is a developing country and health care is of low priority. Thus only when the individuals were seriously inconvenienced (as is likely in malignant lesion) did they seek medical help.

In the present series, spectrum of malignant lesions were very near the figures reported in the other series in literature except for adenocarcinoma, non-hematolymphoid small round cell neoplasm and giant cell carcinoma.

The majority of the lung masses in our series were diagnosed as adenocarcinoma (40.6%), which was very close to the figures quoted by Geraghty P. R. et al (45.6%)<sup>[14]</sup> and Gangopadhyay M. et al (54.2%).<sup>[15]</sup> Two cases (3.1%) were diagnosed as secondary, rest were considered primary. The number of secondaries diagnosed by fine needle aspiration cytology in our study was disproportionately lower than most other workers – Shaheen M. Z. et al (17.6%),<sup>[12]</sup> Geraghty et al (29.1%).<sup>[14]</sup> One of the reasons for this was that the patients with suspected lung secondaries were not referred for FNAC, as the combination of previous case record of malignancy elsewhere and subsequent clinico-radiological features were considered sufficient. The aim of transthoracic fine needle aspiration in such cases is to

confirm that the lung lesion is indeed neoplastic, not inflammatory, and to eliminate the potentially treatable new primary tumours (Johnston et al, 1984).<sup>[16]</sup>

Of all the major types of lung carcinomas, small cell carcinoma was diagnosed least frequently (1.6%) in the current study. This may at first glance seem somewhat surprising in view of the fact that small cell lung carcinoma accounts for about 20% of all lung cancers.<sup>[17]</sup> Review of the cytologic literature reveals frequencies ranging from 1.5% (Ahmed S. et al, 2009)<sup>[18]</sup> to 34.1% (Laurent F. et al, 1999).<sup>[19]</sup> This under-representation in lung FNA smears is probably due to the fact that most cases of small cell lung carcinoma have extrathoracic dissemination at the time of diagnosis and can thus be diagnosed by aspiration from more accessible sites, for example supraclavicular lymphnodes, thus obviating the need for sampling the lung.

In few cases, overlapping of cytological features were seen leading to misdiagnoses that were later corrected by thorough screening of slides, and correlation with clinical features, CT findings and ancillary studies (immunocytochemistry, cytogenetic analysis and electron microscopy) were suggested for definitive diagnosis.

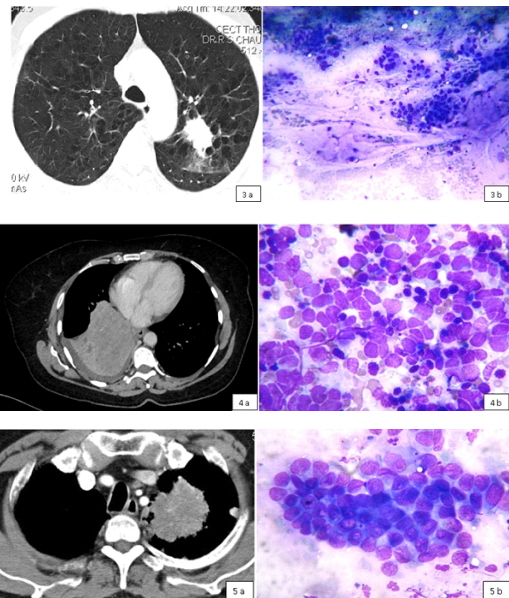
In present study, a solitary case of resolving phase of pneumonia was diagnosed. CT finding was focal lung consolidation, possibly secondary to an underlying mass. So, CT guided FNAC was planned but the centrally located mass could not be accessed and thus the aspirate was from the suspected area of consolidation. Had the FNA been carried out from the centrally located mass, a tumour may have been discovered.

Some smears showed paucity of material, be it normal tissue and/or viable material. This was due to the inability of the needle to reach the centre of the lesion. There was one case which when aspirated on first instance, showed only normal benign epithelium (probably bronchiolar). Later on re-aspiration, the case was diagnosed as adenocarcinoma. In this case the previous aspiration was from the periphery of the tumour (to avoid the necrotic centre) and later re-aspiration was done from the centre of the lesion which procured sufficient material for diagnosis. Later all the smears of previous aspiration was stained; among them, one smear showed features of adenocarcinoma. Hence all smears should be stained to avoid false negative reporting.

Of the 66 cases, 4 cases i.e. 6.1% (on repeat scan after fine needle aspiration) developed pneumothorax. None of the case required intrathoracic chest tube drainage. The pneumothorax rate in different studies reported in the literature varied from 1.5% - 69%. Our results matched the result of Bressler E. L. et al (6%),<sup>[20]</sup> and Zornoza et al (6%).<sup>[21]</sup>

**Conclusion**

It is concluded that C.T. guided FNAC of localized lung lesions is an extremely useful procedure which furnishes adequate and diagnostic material in the vast majority of subjects without significant complications. Cytodiagnostic problems are rather trivial and largely surmountable.

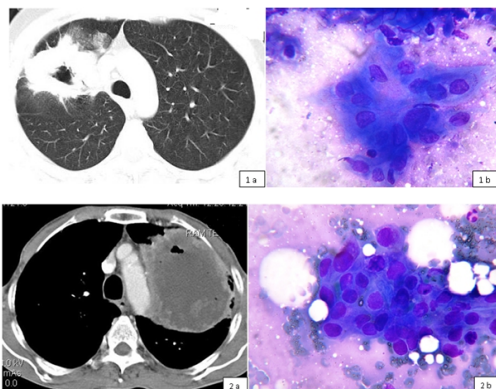


**Legends:**

- Fig. 1a – HRCT chest axial image showing a large ovoid soft tissue density mass lesion with speculated margins seen in right upper lobe and reaching up to the hilum.
- Fig. 1b – Photomicrograph showing well differentiated keratinizing squamous cell carcinoma (MGG, 10X40).
- Fig. 2a – CECT chest axial image showing a large round, peripherally enhancing mass lesion noted in left upper lobe with internal large necrotic areas and a small cavity within.
- Fig. 2b - Photomicrograph showing focus of squamous differentiation in a poorly differentiated squamous cell carcinoma (MGG, 10X40).
- Fig. 3a - HRCT chest axial image showing a ovoid soft tissue density mass lesion with speculated margins present in apico-posterior segment of left upper lobe.
- Fig. 3b - Photomicrograph showing adenocarcinoma : extracellular mucin (MGG, 10X10).
- Fig. 4a - CECT chest axial image showing a heterogeneously enhancing mass lesion in right lower lobe extending upto hilum.
- Fig. 4b - Photomicrograph showing small cell carcinoma : loosely cohesive to dispersed small cells with scanty/ absent cytoplasm, nuclear moulding and apoptotic bodies (MGG, 10X40).
- Fig. 5a - CECT chest axial image showing a ovoid heterogeneously enhancing mass lesion with speculated margins noted in posterior segment of left upper lobe.
- Fig. 5b - Photomicrograph showing adenocarcinoma: cell cluster showing cells with delicate cytoplasm, rounded nuclei with single prominent central nucleoli (MGG, 10X40).

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